Method of Treating Fumarate Hydratase-Deficient Kidney Cancer

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Keywords: Therapeutics, Urinary Organs, Other Technology, tyrosine kinase inhibitor, vandetanib, kidney

Summary:
NCI scientists identified a tyrosine kinase inhibitor vandetanib that is highly cytotoxic to kidney cancer cells both in vitro and in vivo.

Description of Technology:
Patients having germline fumarate hydratase ("FH") gene mutation are predisposed to develop aggressive kidney cancer with few treatment options and poor therapeutic outcomes. NCI scientists identified a tyrosine kinase inhibitor vandetanib that is highly cytotoxic to kidney cancer cells both in vitro and in vivo. C-Abl activity is upregulated in FH-deficient kidney tumors and vandetanib efficacy is a direct consequence of c-Abl inhibition. It was also found that combining metformin enhanced the cytotoxic effect of vandetanib by inhibiting NRF2 transcriptional activity in a SIRT1-dependent manner. Thus dual inhibition of c-Abl and NRF2 activity with vandetanib and metformin is a novel therapeutic approach to target glycolytically dependent, oxidatively stressed tumors. In vitro and in vivo data are available.

Potential Commercial Applications:
Therapies for treating FH-deficient kidney cancer and glycolytically dependent, oxidatively stressed tumors.

Competitive Advantages:
- Specificity of mode of action may reduce potential side-effects -- Novel mode of action may increase market competition -- No effective therapy is currently available for patients with advanced FH-deficient kidney cancer.

Inventor(s):
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Development Stage:
-- Pre-clinical (in vivo)

Publications:
Sourbier C, et al. Targeting ABL1-Mediated Oxidative Stress Adaptation in Fumarate Hydratase-Deficient Cancer. Cancer Cell. 8 December 2014. PMID: 25490448.

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